1-6 have been rejected. Reconsideration is respectfully requested in light of the following remarks.

I. Amendment filed 6-4-02

The Examiner suggests that SEQ ID NO: 2, 4 and 5, which were added by the amendment filed June 4, 2002 were not included in the claims as originally filed. Accordingly, claims 1-6 have only been examined to the extent that they read on SEQ ID NO: 3 and 6.

Applicants respectfully disagree with the Examiner that the claims as originally presented did not encompass SEQ ID NO: 2, 4 and 5. The claims as originally filed were drawn to detecting levels of Lung Specific Genes or LSGs which are defined in the specification at page 6 as meaning levels of the native protein expressed by the gene comprising the polynucleotide sequence of any of SEQ ID NO: 1, 2, 3, 4, 5, or 6, levels of the native mRNA encoded by the gene comprising any of the polynucleotide sequence of SEQ ID NO: 1, 2, 3, 4, 5, or 6, or levels of the gene comprising any of the polynucleotide sequence of SEQ ID NO: 1, 2, 3, 4, 5, or 6. Thus, contrary to the Examiner's suggestions, SEQ ID NO: 2, 4 and 5 were included within the scope of the claims as originally filed and must be examined in the instant application.

II. Rejection of Claims 1-6 under 35 U.S.C. § 112, first paragraph

Claims 1-6 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner has acknowledged the specification to be enabling for a method of diagnosing the presence of lung cancer in patient tissue samples. The Examiner states that the specification provides a clear delineation between the presence or absence of cancer. However, the Examiner suggests that the specification does not reasonably provide enablement for methods of diagnosing metastatic lung cancer, staging lung cancer, monitoring for the onset of metastasis or monitoring changes in stages of lung cancer in any bodily fluid. Specifically, the Examiner suggests that the specification does not provide any qualitative analysis of determining metastasis, staging of lung cancer, monitoring for the onset of metastasis or monitoring for changes in the staging of lung cancer and, absent such teachings, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with these claims.

Applicants respectfully traverse this rejection.

MPEP is quite clear; a specification disclosure which

contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is reason to doubt the objective truth of statements contained in therein which must be relied on for enabling support. Detailed teachings for determining metastasis via the present invention are described in the specification at pages 7-8. Detailed teachings for staging of lung cancer via the present invention are described in the specification at pages 8-9. Detailed teachings for monitoring for the onset of metastasis via the present invention are described in the specification at page 9. Detailed teachings for monitoring for changes in the staging of lung cancer via the present invention are also described in the specification at page 9. Further, assay techniques for detecting levels of LSGs for use in the methods of the present invention are described in detail in the specification at pages 9-12. Accordingly, the instant specification clearly contains a teaching of the manner and process of using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented.

Further, in accordance with MPEP § 2164.04, in order to make a lack of enablement rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. As stated by the court in *In re Marzocchi*, 439 F.2d 220,169 USPQ 367 (CCPA 1971), "[i]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." Reasoning provided by the Examiner in the instant rejection is insufficient to meet this burden.

The broad statement of Lau et al. (2000) that "clinical staging has limitations" relied upon by the Examiner hardly provides the requisite evidence or reasoning to doubt the accuracy of statements in the specification that detecting levels of an LSG of the present invention is useful in determining metastasis, staging of lung cancer, monitoring for the onset of metastasis or monitoring for changes in the staging of lung cancer.

Moreover, Chuman et al. (FEBS Letters 1999 462:129-134), considered by the Examiner in the Information Disclosure

Statement filed April 11, 2002, provides contradicting evidence to the teachings of Lau et al. Chuman et al. disclose that one of the Lung Specific Genes of the present invention, namely Napsin A, was detected by 2-dimensional electrophoresis in a high percentage of clinically observed lung adenocarcinomas. Further, Chuman et al. characterize Napsin A as "a useful marker in the differential diagnosis between primary and metastatic lung adenocarcarcinomas." See the Discussion in Chuman et al. at page 133. In addition, Chuman et al. teach the highly restricted expression in lung tissue, thus suggestive of detection of expression elsewhere being indicative of metastasis that originated from lung cancer. Thus, the disclosure of Chuman et al. corroborates the teachings of the instant application that the Lung Specific Genes of the present invention are useful in determining metastasis, staging of lung cancer, monitoring for the onset of metastasis, and monitoring for changes in the stage of lung cancer.

While the publication date of Chuman et al. is subsequent to the filing date of the present invention and therefore is not a valid prior art reference with respect to the instant application, its teachings clearly indicate that the reference by Lau et al. published in 2000 is not representative of the

general understanding in this art. Accordingly, Applicants also respectfully disagree with the Examiner's suggestion that the broad teaching of Lau et al. serves as a representation of the state of the relevant art or that this reference is indicative of predictability or lack thereof in the art. In accordance with MPEP § 2164.03 the "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, than there is predictability in the art. The Examiner has acknowledged the instant specification to provide working examples of a positive or negative determination of lung cancer in cells and tissues. The Examiner has also acknowledged the instant specification to provide a clear delineation between the presence or absence of cancer. Clearly, one of skill in the art, with the specification in hand, has the ability to extrapolate the disclosed results to further use in staging and monitoring lung cancer. One skilled in the art can readily anticipate based upon the teachings of the specification that an increase in an LSG as claimed in indicative of metastasis and/or a cancer progressing in stage while a decrease in an LSG is indicative of

the cancer regressing. Thus, contrary to the Examiner's suggestion, there is predictability in this invention based upon the teachings of the specification.

Finally, Examiner's suggestion that a working example or qualitative analysis of determining metastasis, staging of lung cancer, monitoring for the onset of metastasis or monitoring for changes in the staging of lung cancer is required also improper. MPEP 2164.02 clearly states that "[c]ompliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether an example is disclosed. Further, MPEP § 2164.02 states that lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement.

Accordingly, withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

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favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

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